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Case Report

Active cardiac sarcoidosis in a patient with adult-onset Kawasaki disease

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ABSTRACT

Adult-onset Kawasaki disease is a rare condition. Cardiac sarcoidosis is an uncommon cardiomyopathy which is characterized by progressive cardiac dysfunction, and abnormality on electrocardiography and morphological aberration of the heart. We report a first case of a combination of these rare conditions. The patient was initially diagnosed with Kawasaki disease based on the coronary artery aneurysms and a past medical history at the age of 20 years which was typical of Kawasaki disease. Decades later, he developed progressive cardiac dysfunction and a sudden-onset atrioventricular block. Laboratory and imaging results revealed severe myocardial damage and inflammation which were unexplainable by coronary artery ischemia. We diagnosed him with cardiac sarcoidosis based on a Japanese guideline to diagnose cardiac sarcoidosis. A cardiac resynchronization therapy defibrillator was implanted and he received oral steroid therapy. This rare combination of adult-onset Kawasaki disease and cardiac sarcoidosis may suggest the causative association of these conditions.

<**Learning objective:** This is the first report of a rare combination of adult-onset Kawasaki disease and cardiac sarcoidosis. Kawasaki disease is not just a disease of children. Physicians should include Kawasaki disease in the list of differentials for unknown fever or eruptions. In patients with progressive heart failure and atrioventricular block, the possibility of cardiac sarcoidosis should be examined using various imaging modalities even if they had a known cause of cardiac dysfunction.>

Introduction

Kawasaki disease is a type of vasculitis which preferentially affects children. Kawasaki disease can occur rarely in an adult. A previous report showed that coronary aneurysm occurs in 5% of patients with adult-onset Kawasaki disease, and the patients often suffered from ischemic complications, leading to severe ischemic cardiomyopathy [1].

Cardiac sarcoidosis, which is a granulomatous disease of unknown etiology characterized by non-caseating granulomas in involved organs, is also rare and difficult to diagnose because of its various clinical courses. In fact, only 40–50% of patients with cardiac sarcoidosis diagnosed at autopsy have the correct diagnosis made during their lifetime [2]. The most common presented findings of cardiac sarcoidosis are progressive ventricular dysfunction and arrhythmia, including mainly atrioventricular block.

In the current report, we present an extremely rare combination of adult-onset Kawasaki disease and cardiac sarcoidosis. This case tells us one should suspect cardiac sarcoidosis in case of progressive cardiac dysfunction and atrioventricular block even in the patients with a known cause of cardiac dysfunction.

Case report

A 58-year-old man with a following past medical history came to the emergency room with dyspnea worsening over the previous 4 days.

At the age of 20 years, he suffered from a high fever sustained for 18 days, polymorphous rash, cervical lymphadenopathy, strawberry tongue, and desquamation of the hands. He was treated with some intravenous antibiotics as for a bacterial infectious disease, but antibiotics were not effective. About half a

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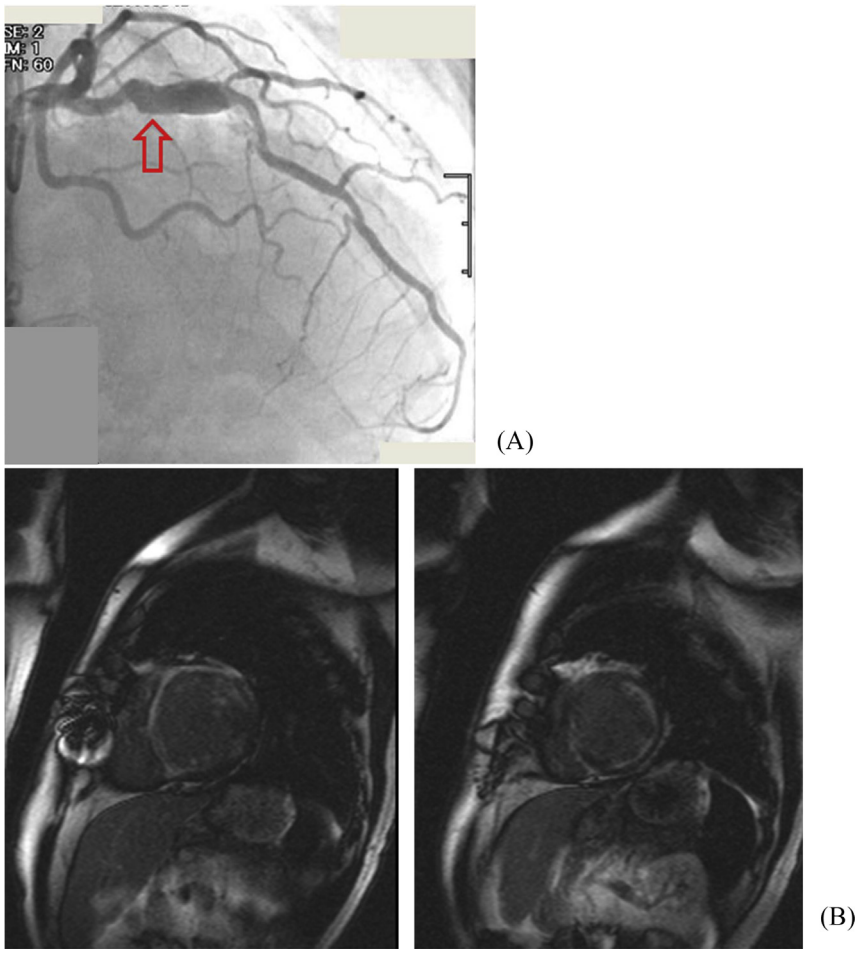

Fig. 1. (A) Coronary angiography shows coronary artery aneurysm at left anterior descending artery #6. (B) Cardiac magnetic resonance imaging with gadolinium transmural and patchy-delayed enhancement in diffuse left ventricle myocardium.

month later, symptoms spontaneously resolved. At the age of 48 years, he was diagnosed with Kawasaki disease based on his past medical history at the age of 20 years and coronary angiography (CAG) showing coronary artery aneurysm with severe calcification on the proximal portion of the left anterior descending artery (Fig. 1A). At the age of 55 years, he was found to have complete right bundle branch block and first-degree atrioventricular block on an electrocardiogram (ECG) tracing, but his left ventricular function was preserved at that time [left ventricular ejection fraction (LVEF): 57%]. The next year, he developed heart failure with left ventricular dysfunction (left ventricular diastolic dimension/systolic dimension: 61/47 mm, LVEF: 36%, CAG: #1 100%, #6 aneurysm, #7 75%) and severe mitral regurgitation. He underwent coronary bypass graft surgery (a graft using left internal thoracic artery to left anterior descending artery; sequential grafts using radial artery to first diagonal branch and #4 posterior descending artery), mitral valve repair, and tricuspid annuloplasty. Despite successful surgical procedure, left ventricular function did not improve except for some decrease in the left ventricular diastolic dimension (diastolic dimension/systolic dimension: 56/47 mm, LVEF: 30%).

Six months after the cardiac operation, he developed dyspnea. On admission, inspiratory rales were heard at both lungs with oxygen saturations of 90% on room air. There were a protodiastolic gallop and grade 2 systolic murmur in the 4th left intercostal space. He was diagnosed with acute decompensated heart failure [New York Heart Association (NYHA) class IV] in the emergency room, and was immediately treated with oxygen and intravenous diuretics. Blood sample investigations revealed that the serum level of B-type natriuretic peptide was 1284 pg/mL (normal: <18.4 pg/mL), and troponin T 0.044 ng/mL (normal: <0.014 ng/mL). ECGs showed a tri-fascicular block (left axis deviation, first-degree atrioventricular block, and complete right bundle branch block), and wide QRS duration (170 ms). A monitor ECG revealed non-sustained ventricular tachycardia. A transthoracic echocardiogram showed severely reduced left ventricular function (LVEF: 17%) and abnormal septal wall thinning (wall thickness <6 mm). CAG proved patency of bypass graft. Dyspnea improved 3 days after admission. However, he suffered from paroxysmal dyspnea, and an ECG monitor tracing showed an advanced atrioventricular block at 12th day after hospitalization. He received a transvenous temporary pacemaker.

The serum level of angiotensin-converting enzyme was 31.3 U/L (normal: 7.7–29.4 U/L). Tuberculin test turned negative, and there was no obvious sign of uveitis. Computed tomography showed bilateral hilar lymphadenopathy. A cardiac magnetic resonance imaging showed a broad damage of the cardiac tissue, which did not follow the coronary artery distribution (Fig. 1B). 67Gallium scintigraphy and fluorodeoxyglucose (FDG)-positron emission tomography (PET) revealed broad inflammation of the cardiac tissue (Fig. 2A and B). FDG-PET also showed bilateral hilar lymphadenopathy (Fig. 2C). He underwent a right ventricular endomyocardial biopsy. The pathological analyses proved fibrotic changes in myocardium, but no non-caseating epithelioid cell

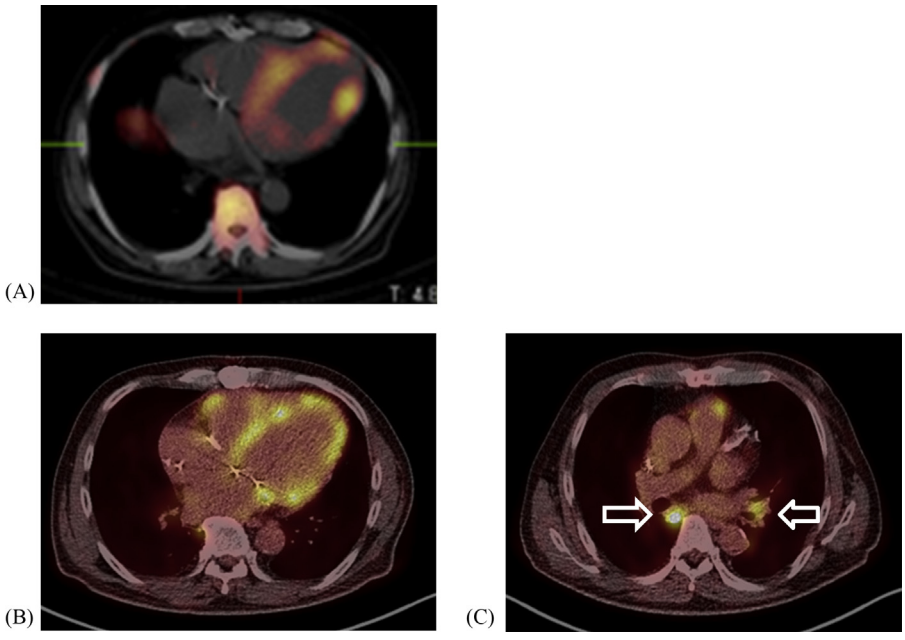

Fig. 2. (A) 67Gallium scintigraphy reveals intense myocardial uptake of gallium all around myocardium without apex and basal-lateral wall. (B and C) Fluorodeoxyglucose-positron emission tomography was positive in myocardium especially basal-septal and anterior wall [standardized uptake value (SUV)max7.2] (B), and in bilateral hilar lymphadenopathy (arrow) (SUVmax6.8) (C).

granulomas. Before admission he was prescribed aspirin 100 mg, furosemide 20 mg, omeprazole 15 mg, nicorandil 15 mg, and rosuvastatin 2.5 mg.

Past history was suggestive of ischemic cardiomyopathy due to Kawasaki disease. However, the distribution of myocardial damage did not match the coronary artery distribution. Endomyocardial biopsy findings did not suggest other cardiomyopathy and myocarditis. We finally diagnosed him as having cardiac sarcoidosis complicated with Kawasaki disease.

A cardiac resynchronization therapy defibrillator was implanted, and he received the standard medical therapy including an oral β-blocker. He also received an oral steroid therapy (30 mg/day) in order to inhibit the progressive impairment of cardiac function. The patient was in NYHA class II and the serum level of B-type natriuretic peptide was decreased to 286 pg/ml. There were no advanced atrioventricular block and exacerbation of cardiac function (LVEF: 24%) after treatment with steroid.

Discussion

This is the first report of a combination of adult-onset Kawasaki disease and cardiac sarcoidosis. Because both the conditions are relatively rare, it is warranted to carefully discuss the diagnoses of them.

Kawasaki disease is a childhood vasculitis especially affecting the coronary artery. Over 90% of cases occur in young children and infants. Adult-onset Kawasaki disease has been rarely reported, most cases occur between the age of 18 and 30 years [3]. In the current case, the patient presented symptoms typical of Kawasaki disease at the age of 20 years: (1) fever >14 days, (2) polymorphous rash, (3) cervical lymphadenopathy, (4) oral changes including injected lips and strawberry tongue, (5) extremity changes starting with edema, then progressing to desquamation of the hands starting periungually. Despite typical symptoms, the correct diagnosis was not made at that time. There are several clinical differences between pediatric and adult cases of Kawasaki disease. Coronary artery aneurysm formation was reported in about 20% of pediatric cases, but only 5% of adult cases [1]. However, like a pediatric case, coronary angiography and treatment for cardiac ischemia are important to avoid life-threatening events caused by cardiac ischemia in adult cases.

The prevalence of sarcoidosis is 10–40/100,000 persons in the USA and Europe. However, there are some regional differences in prevalence. A previous report showed that clinically evident cardiac involvement sarcoidosis is 3–5% [4]. In pathology series, cardiac involvement in sarcoidosis occurs in 20–79% of patients [5,6]. In Japanese patients with sarcoidosis, cardiac involvement may be as high as about 60%, but only about 40% of patients with cardiac sarcoidosis at autopsy have the correct diagnosis made during their lifetime [2,5,6]. A definite diagnosis of cardiac sarcoidosis is made by endomyocardial biopsy. However, the sensitivity of endmyocardial biopsy for non-caseating granulomas is usually less than 20%, because of its patchy myocardial involvement [7]. On account of its low sensitivity, cardiac sarcoidosis has often been diagnosed clinically based on other clinical findings, including progressive heart failure, atrioventricular block, biomarkers, and various imaging modalities detecting cardiac damage. The guideline for diagnosis of sarcoidosis requires evidence of multiple organs involved for definite clinical diagnosis in the absence of non-caseating granulomas from biopsy (Table 1) [8]. We clinically diagnosed the present case as being cardiac sarcoidosis based on the various cardiac findings as well as bilateral hilar lymphadenopathy, which was strongly suggestive of lung sarcoidosis. PET and radionuclide scan have been known to be useful to detect myocardial damage and inflammation (Fig. 2). Recent reports showed that cardiac magnetic resonance imaging reveals the lesion affected by sarcoidosis. Surprisingly, delayed hyperenhancement represents myocardium that has been replaced by the fibrogranulomatous tissue, and it can detect even the inactive lesion affected by sarcoidosis (Fig. 1B) [9,10].

The etiological association between Kawasaki disease and sarcoidosis has not been known. In a previous article, *Propionibacterium acnes* has been reported as a potentially common causative agent of these diseases based on pathological examinations

Table 1 Guidelines for diagnosing cardiac sarcoidosis 2006 (Japan Society of Sarcoidosis and Other Granulomatous Disorders).

Histologic diagnosis group
Endomyocardial biopsy demonstrates non-caseating granuloma in addition to the histologic or clinical diagnosis of extracardiac sarcoidosis.
Clinical diagnosis group
Extracardiac sarcoidosis is diagnosed histologically or clinically and satisfies the following conditions (at least 2 of 4 major criteria, or one of 4 major criteria and at least 2 of 5 minor criteria are satisfied) and more than one in six basic diagnostic criteria.
Major criteria
(a) Advanced atrioventricular block.
(b) Basal thinning of intraventricular septum.
(c) Positive cardiac 67Ga uptake.
(d) Depressed ejection fraction of the left ventricle (LVEF < 50%).
Minor criteria
(a) Abnormal ECG findings: ventricular arrhythmias (VT, multifocal or frequent PVCs), CRBBB, axis deviation, or abnormal Q-wave.
(b) Abnormal echocardiography: regional abnormal wall motion or morphological abnormality (ventricular aneurysm, wall thinning).
(c) Nuclear medicine: perfusion defect detected by 201Tl myocardial scintigraphy or 99Tc myocardial scintigraphy.
(d) Gd-enhanced MRI: delayed enhancement of myocardium.
(e) Endomyocardial biopsy: interstitial fibrosis or monocyte infiltration over moderate grade.
Basic criteria
(a) Bilateral hilar lymphoadenopathy.
(b) Elevation of angiotensin-converting enzyme.
(c) Negative of tuberculin test.
(d) Positive 67Ga uptake.
(e) Elevation of CD4/CD8 ratio in bronchoalveolar lavage.
(f) Elevation of serum and urine calcium.

ECG, electrocardiogram; LVEF, left ventricular ejection fraction; MRI, magnetic resonance imaging; PVC, premature ventricular contraction; CRBBB, complete right bundle branch block; VT, ventricular tachycardia.

[11]. However, Ishige et al. [12] reported that *Propionibacterium acnes* resided in normally peripheral lung tissue. Thus, the relationship between *Propionibacterium acnes* and these diseases remains undetermined. Further studies are needed to confirm this hypothesis.

This case represents an unusual association of rare diseases, adult-onset Kawasaki disease and cardiac sarcoidosis. This case tells us one should suspect cardiac sarcoidosis in case of progressive cardiac dysfunction and atrioventricular block even in the patients with a known cause of cardiac dysfunction.

Conflict of interest

None.

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